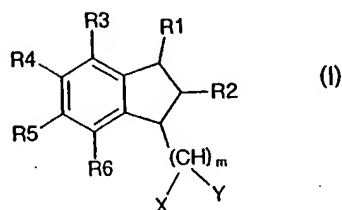


WHAT IS CLAIMED IS:

1. A compound having structural formula (I):



stereoisomers thereof, or pharmaceutically acceptable salts or hydrates thereof, wherein:

**R1**, and **R2** are selected from the group comprising:

- i) H
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol and  $-(CH_2)_n$ -isoxazol, where  $n=1, 2, 3, 4, 5$ , or  $6$ ;

**X** is an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol and isoxazol;

**Y** is a basic group selected from the group comprising  $1^\circ$  amino,  $2^\circ$  amino,  $3^\circ$  amino, quaternary ammonium salts, aliphatic  $1^\circ$  amino, aliphatic  $2^\circ$  amino, aliphatic  $3^\circ$  amino, aliphatic quaternary ammonium salts, aromatic  $1^\circ$  amino, aromatic  $2^\circ$  amino, aromatic  $3^\circ$  amino, aromatic quaternary ammonium salts, imidazol, guanidino, boronoamino, allyl, urea and thiourea;

**m** is 0, 1; and

**R3**, **R4**, **R5**, **R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof;

with the proviso:

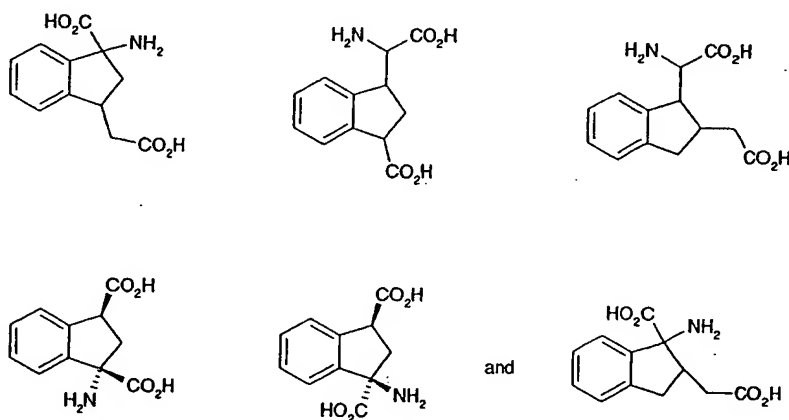
- i) when **X** is COOH, **Y** is  $NH_2$ ,  $R3=R4=R5=R6=H$ , then both **R1** and **R2** are not H at the same time;

ii) when  $n=0$ , X is COOH, Y is NH<sub>2</sub>, R<sub>1</sub>=R<sub>2</sub>=R<sub>6</sub>=H and one of the groups R<sub>3</sub>, R<sub>4</sub> or R<sub>5</sub> is COOH, then the remaining two groups of R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are not both H at the same time.

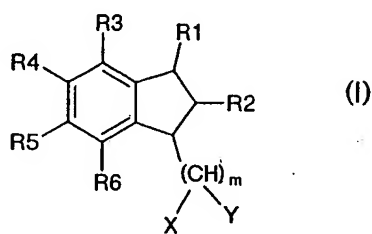
2. The compound according to claim 1, wherein **R1** is H, CO<sub>2</sub>H or CH<sub>2</sub>CO<sub>2</sub>H.

3. The compound according to claim 1, wherein **R2** is H, CO<sub>2</sub>H, or CH<sub>2</sub>CO<sub>2</sub>H.

4. The compound according to claim 1, wherein said compound is selected from the group of compounds:



5. A process for the preparation of a compound of Formula I:



or a pharmaceutically acceptable metabolically-labile ester or amide thereof, or a pharmaceutically acceptable salt thereof; wherein:

**R1**, and **R2** are selected from the group comprising:

- i) H
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfinio, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -

phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfonyl,  $-(CH_2)_n$ -sulfinyl,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol and  $-(CH_2)_n$ -isoxazol, where  $n=1, 2, 3, 4, 5$ , or  $6$ ;

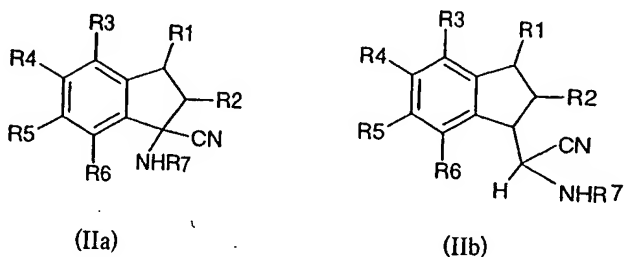
**X** is an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfonyl, sulfinyl, borono, tetrazol and isoxazol;

**Y** is a basic group selected from the group comprising 1° amino, 2° amino, 3° amino, quaternary ammonium salts, aliphatic 1° amino, aliphatic 2° amino, aliphatic 3° amino, aliphatic quaternary ammonium salts, aromatic 1° amino, aromatic 2° amino, aromatic 3° amino, aromatic quaternary ammonium salts, imidazol, guanidino, boronoamino, allyl, urea and thiourea;

**m** is 0, 1; and

**R3, R4, R5, R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof; which comprises:

b) hydrolyzing a compound of formula (IIa) or (IIb):

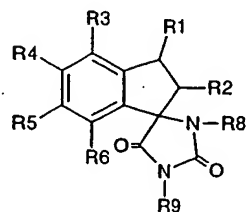


wherein: **R1**, and **R2** are selected from the group comprising:

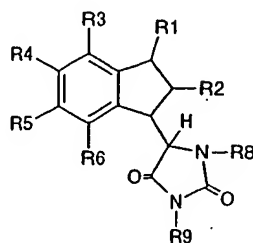
- i) H
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfonyl, sulfinyl, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfonyl,  $-(CH_2)_n$ -sulfinyl,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol and  $-(CH_2)_n$ -isoxazol, wherein  $n=1, 2, 3, 4, 5$ , or  $6$ ; and

**R3, R4, R5 and R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof, **R7** is a hydrogen atom or an acyl group. Preferred functional groups for **R7** are hydrogen and C<sub>2</sub>-C<sub>6</sub> alkanoyl groups, such as acetyl; or

c) hydrolyzing a compound of formula (IIIa) or (IIIb):



(IIIa)

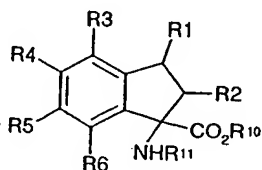


(IIIb)

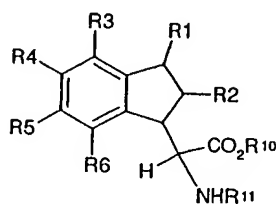
wherein:

**R1, R2, R3, R4, R5 and R6** are as defined above, **R8 and R9** are each independently represent a hydrogen atom, a (C<sub>2</sub>-C<sub>6</sub>) alkanoyl group, a (C<sub>1</sub>-C<sub>4</sub>) alkyl group, a (C<sub>3</sub>-C<sub>4</sub>) alkenyl group or a phenyl (C<sub>1</sub>-C<sub>4</sub>) alkyl group wherein the phenyl is unsubstituted or substituted by halogen, (C<sub>1</sub>-C<sub>4</sub>) alkyl or (C<sub>1</sub>-C<sub>4</sub>) alkoxy, or a salt thereof; or

d) deprotecting a compound of formula (IVa) or (IVb)



(IVa)



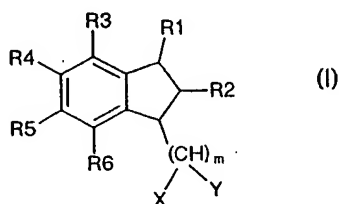
(IVb)

wherein: **R1**, **R2**, **R3**, **R4**, **R5** and **R6** are as defined above and **R10** is a hydrogen atom or a carboxyl protecting group, or a salt thereof, and **R11** represents a hydrogen atom or a nitrogen protecting group;

whereafter, if necessary and/or desired, the following steps are carried out:

- (i) resolving the compound of Formula I;
- (ii) converting the compound of Formula I into a non-toxic metabolically labile ester or amide thereof and/or;
- (iii) converting the compound of Formula I or a non-toxic metabolically labile ester or amide thereof into a pharmaceutically acceptable salt thereof.

6. A pharmaceutical composition comprising a pharmaceutically acceptable carrier, diluent or excipient, and a compound of structural formula (I):



or stereoisomers thereof, or pharmaceutically acceptable salts or hydrates thereof, wherein:

**R1**, and **R2** are selected from the group comprising:

- i) H
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol, and  $-(CH_2)_n$ -isoxazol, where  $n=1, 2, 3, 4, 5$ , or  $6$ ;

**X** is an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, and isoxazol;

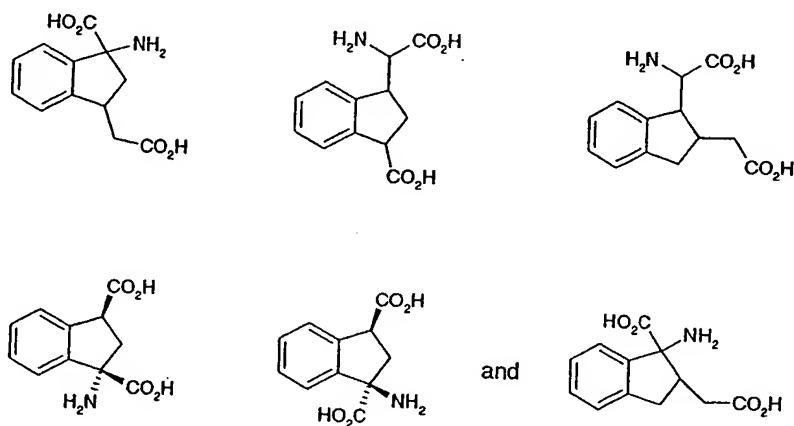
**Y** is a basic group selected from the group comprising  $1^\circ$  amino,  $2^\circ$  amino,  $3^\circ$  amino, quaternary ammonium salts, aliphatic  $1^\circ$  amino, aliphatic  $2^\circ$  amino, aliphatic  $3^\circ$  amino, aliphatic quaternary

ammonium salts, aromatic 1° amino, aromatic 2° amino, aromatic 3° amino, aromatic quaternary ammonium salts, imidazol, guanidino, boronoamino, allyl, urea and thiourea;

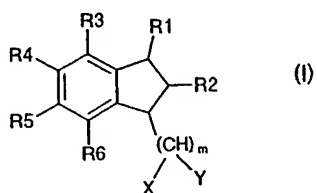
**m** is 0, 1; and

**R3, R4, R5, R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof.

7. The pharmaceutical composition of claim 6, wherein said compound is selected from the group of compounds:



8. A use of an effective amount of a compound of structural formula (I):



or stereoisomers thereof, or pharmaceutically acceptable salts or hydrates thereof, in modulating one or more metabotropic glutamate receptor functions in warm blooded mammals, wherein said use comprises administering an effective amount of a compound of formula (I); wherein:

**R1** and **R2** are selected from the group comprising:

- i) H
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfinio, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfinio,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol, and  $-(CH_2)_n$ -isoxazol, where  $n=1, 2, 3, 4, 5$ , or  $6$ ;

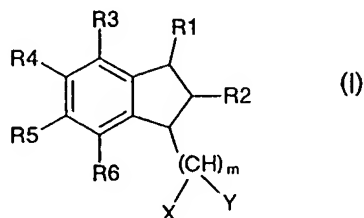
**X** is an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfinio, borono, tetrazol and isoxazol;

**Y** is a basic group selected from the group comprising  $1^\circ$  amino,  $2^\circ$  amino,  $3^\circ$  amino, quaternary ammonium salts, aliphatic  $1^\circ$  amino, aliphatic  $2^\circ$  amino, aliphatic  $3^\circ$  amino, aliphatic quaternary ammonium salts, aromatic  $1^\circ$  amino, aromatic  $2^\circ$  amino, aromatic  $3^\circ$  amino, aromatic quaternary ammonium salts, imidazol, guanidino, boronoamino, allyl, urea and thiourea;

**m** is 0, 1; and

**R3**, **R4**, **R5**, **R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl and pharmaceutically acceptable ester or salt thereof,

9. A use of an effective amount of a compound of structural formula (I):



or stereoisomers thereof, or pharmaceutically acceptable salts or hydrates thereof, in treating a neurological disease or disorder selected from the group comprising:

cerebral deficits subsequent to cardiac bypass surgery and grafting, cerebral ischemia, stroke, cardiac arrest, spinal cord trauma, head trauma, perinatal hypoxia, and hypoglycemic neuronal damage, Alzheimer's disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, ocular damage, retinopathy, cognitive disorders, idiopathic and drug-induced Parkinson's disease, muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, drug tolerance, withdrawal and cessation (i.e. opiates, benzodiazepines, nicotine, cocaine, or ethanol), smoking cessation, anxiety and related disorders (e.g. panic attack), emesis, brain edema, chronic pain, sleep disorders, Tourette's syndrome, attention deficit disorder, and tardive dyskinesia, wherein said use comprises administering an effective amount of a compound of formula (I);

wherein: **R1**, and **R2** are selected from the group comprising:

- i) H
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol, and  $-(CH_2)_n$ -isoxazol, where  $n=1, 2, 3, 4, 5$ , or  $6$ ;

**X** is an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol and isoxazol;

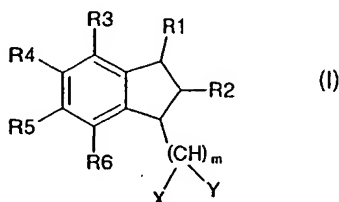
**Y** is a basic group selected from the group comprising  $1^\circ$  amino,  $2^\circ$  amino,  $3^\circ$  amino, quaternary ammonium salts, aliphatic  $1^\circ$  amino, aliphatic  $2^\circ$  amino, aliphatic  $3^\circ$  amino, aliphatic quaternary ammonium salts, aromatic  $1^\circ$  amino, aromatic  $2^\circ$  amino, aromatic  $3^\circ$  amino, aromatic quaternary ammonium salts, imidazol, guanidino, boronoamino, allyl, urea and thiourea;

**m** is 0, 1; and



**R3, R4, R5, R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof.

10. A use of an effective amount of a compound of structural formula (I):



or stereoisomers thereof, or pharmaceutically acceptable salts or hydrates thereof, in treating a psychiatric disease or disorder selected from the group comprising: schizophrenia, anxiety and related disorders (e.g. panic attack), depression, bipolar disorders, psychosis, and obsessive compulsive disorders, wherein said use comprises administering an effective amount of a compound of formula (I);

wherein: **R1**, and **R2** are selected from the group comprising:

- i) H
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol and  $-(CH_2)_n$ -isoxazol, where n=1, 2, 3, 4, 5, or 6;

**X** is an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol and isoxazol;

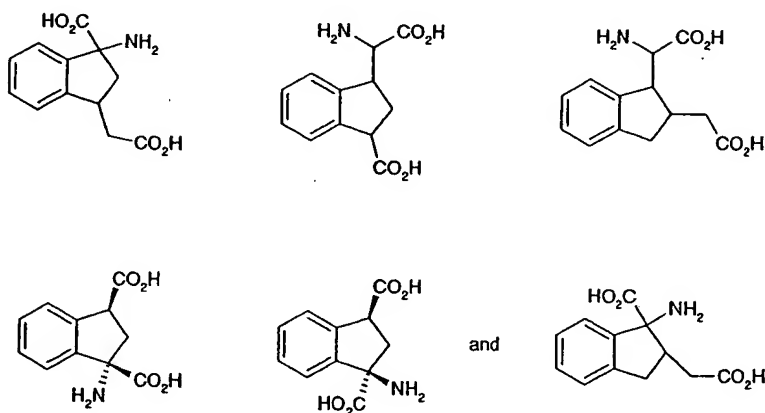
**Y** is a basic group selected from the group comprising 1° amino, 2° amino, 3° amino, quaternary ammonium salts, aliphatic 1° amino, aliphatic 2° amino, aliphatic 3° amino, aliphatic quaternary

ammonium salts, aromatic 1° amino, aromatic 2° amino, aromatic 3° amino, aromatic quaternary ammonium salts, imidazol, guanidino, boronoamino, allyl, urea and thiourea;

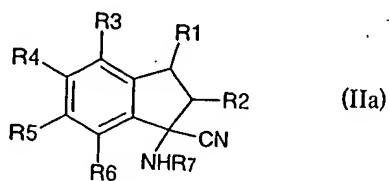
**m** is 0, 1; and

**R3, R4, R5, R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof.

11. The use according to any one of claims 8, 9 and 10 wherein said compound is selected from the group of compounds comprising:



12. A compound of formula (IIa):

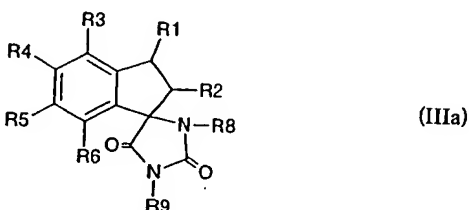


wherein: **R1**, and **R2** are selected from the group consisting of:

- i) H;
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol and  $-(CH_2)_n$ -isoxazol, where  $n=1, 2, 3, 4, 5$ , or  $6$ ;

**R3**, **R4**, **R5** and **R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof, **R7** is a hydrogen atom or an acyl group. Preferred functional groups for **R7** are hydrogen and (C<sub>2</sub>-C<sub>6</sub>) alkanoyl groups, such as acetyl.

13. A compound of formula (IIIa):



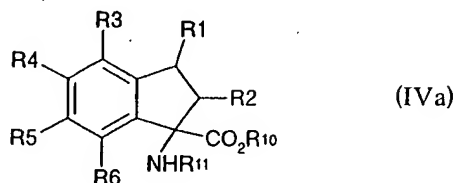
wherein: wherein: **R1** and **R2** are selected from the group consisting of:

- i) H;
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol and  $-(CH_2)_n$ -isoxazol, where  $n=1, 2, 3, 4, 5$ , or  $6$ ;

**R3**, **R4**, **R5** and **R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof; **R8** and **R9** are each independently represent a hydrogen atom, a (C<sub>2</sub>-C<sub>6</sub>) alkanoyl group, a (C<sub>1</sub>-C<sub>4</sub>) alkyl group, a (C<sub>3</sub>-C<sub>4</sub>) alkenyl group or a phenyl (C<sub>1</sub>-C<sub>4</sub>) alkyl group wherein the

phenyl is unsubstituted or substituted by halogen, (C<sub>1</sub>-C<sub>4</sub>) alkyl or (C<sub>1</sub>-C<sub>4</sub>) alkoxy, or a salt thereof.

14. A compound of formula (IVa):



wherein: wherein: wherein: **R1**, and **R2** are selected from the group consisting of:

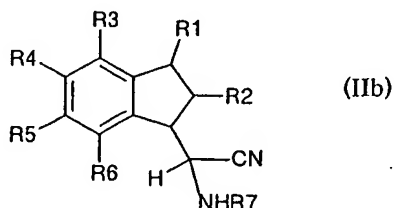
- i) H
- iii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol and  $-(CH_2)_n$ -isoxazol, where  $n=1, 2, 3, 4, 5$ , or  $6$ ;

**R3**, **R4**, **R5** and **R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof; **R10** is a hydrogen atom or a carboxyl protecting group, or a salt thereof, and **R11** is a hydrogen atom or a nitrogen protecting group;

with the proviso, when  $R1=R2=R3=R4=R5=R6=H$  and:

- i) **R11** is H then **R10** is other than methyl or ethyl; or
- ii) **R11** is  $-CO_2CH_2C_6H_5$  then **R10** is other than H or  $CH_3$ .

15. A compound of formula (IIb):

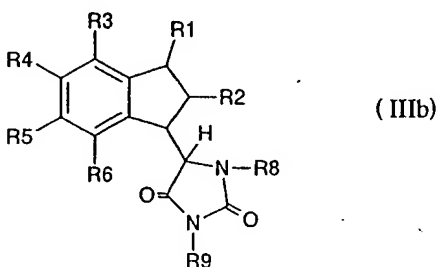


wherein: wherein: wherein: **R1** and **R2** are selected from the group consisting of:

- i) H
- iv) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol and  $-(CH_2)_n$ -isoxazol, where  $n=1, 2, 3, 4, 5$ , or  $6$ ;

**R3**, **R4**, **R5** and **R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof; **R7** is a hydrogen atom or an acyl group. Preferred functional groups for **R7** are hydrogen and  $(C_2-C_6)$  alkanoyl groups, such as acetyl.

16. A compound of formula (IIIb):



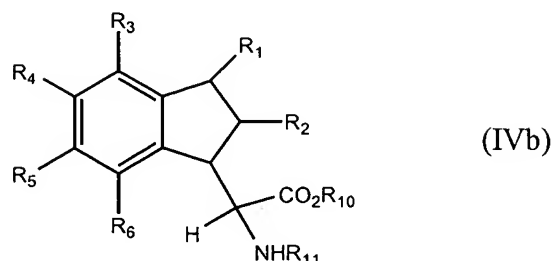
wherein: **R1**, and **R2** are selected from the group consisting of:

- i) H
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol and  $-(CH_2)_n$ -isoxazol, where  $n=1, 2, 3, 4, 5$ , or  $6$ ;

**R3**, **R4**, **R5** and **R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof; **R8** and **R9** are each independently represent a hydrogen atom, a  $(C_2-C_6)$  alkanoyl group, a  $(C_1-C_4)$  alkyl group, a  $(C_3-C_4)$  alkenyl group or a phenyl  $(C_1-C_4)$  alkyl group wherein the

phenyl is unsubstituted or substituted by halogen, (C<sub>1</sub>-C<sub>4</sub>) alkyl or (C<sub>1</sub>-C<sub>4</sub>) alkoxy, or a salt thereof.

17. A compound of formula (IVb):



wherein: wherein: wherein: **R1** and **R2** are selected from the group consisting of:

- i) H.
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfinio, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfinio,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol and  $-(CH_2)_n$ -isoxazol, where  $n=1, 2, 3, 4, 5$ , or  $6$ ;

**R3**, **R4**, **R5** and **R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof; **R10** is a hydrogen atom or a carboxyl protecting group or a salt thereof, and **R11** is a hydrogen atom or a nitrogen protecting group;

with the proviso, when  $R1=R2=R3=R4=R5=R6=R10=H$ , then **R11** is other than  $CO_2t\text{-Bu}$ .